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Case Report

Histological surprise, mammary analogue secretory carcinoma of parotid gland

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ABSTRACT

A recent described entity, mammary analogue secretary carcinoma (MASC) in 2010 by Skalova et al whose morphological and immunohistochemical features are similar in secretory carcinoma of the breast and salivary gland. This is a low-grade carcinoma which presents as a firm, slow-growing, circumscribed lesion with male preponderance. We present a case report of MASC.

Keywords: Mammary analogue secretary carcinoma, MASC, Parotid gland, parotidectomy

INTRODUCTION

The normal breast and salivary glands derive it's origin from same embryonic ectoderm. They share similar architecture (ductulo-acinar) and cellular composition (luminal epithelial cells surrounded by myoepithelial cells). Hence both have similar morphology and immuno profile. These features attribute to development of similar neoplastic lesions. Secretary carcinoma is a low-grade invasive carcinoma composed of epithelial cells with intra cytoplasmic secretary vacuoles and extra cellular Eosinophilic bubbly secretions arranged in variable architecture. These tumours are frequently associated with ETV6-NTRK3 fusions. Mammary analogue secretory carcinoma (MASC) of the salivary gland is a recently described entity that has just been established in the new World Health Organization (WHO) classification of head and neck tumours (4th edition, 2017). Secretory carcinoma was first documented in salivary glands in 2010 by Skalov et al in a series of 16 cases.[1] Secretory carcinoma of the breast (SC) and MASC found elsewhere have shown a characteristic recurrent balanced chromosomal translocation t(12;15) (p13;q25), resulting in ETV6-NTRK3 oncogenic fusion gene. Present in both in situ and invasive component indicating this to be an early event in tumourigenesis. This fusion gene encodes a chimeric tyrosine kinase that is known to play an important role on its oncogenesis through the RAS-NAPK and P13K pathway.[2] We present a case report of 61-year-old male with left pre auricular region swelling.

CASE REPORT

A 61-year-old gentleman presented with a left pre-auricular swelling since 6 years which was initially small and gradually progressed to the present size of 3×4 cm. There was no increase or decrease in size of swelling on chewing. No history of sudden increase in size of the swelling. Swelling was not associated with pain. No difficulty in opening mouth, chewing and closing eyes. No history of drooling of saliva from angle of mouth.

General physical examination

General physical examination were elderly male, well-built. vitals-within normal limits. no pallor, icterus, cyanosis, clubbing or lymphadenopathy.

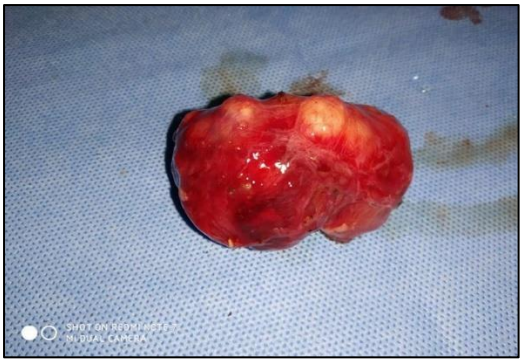

Figure 1: Excised specimen of parotid with modular surface.

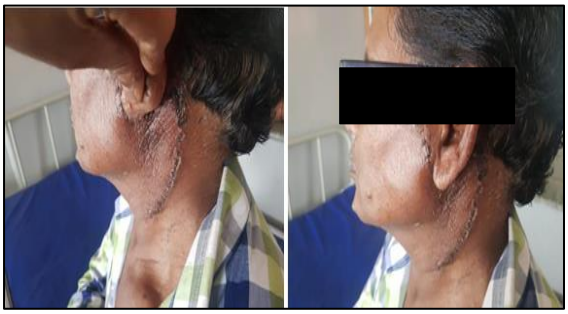

Figure 2: Post operative pictures of the patient.

Figure 3: Demonstrating intact facial nerve following surgery.

System examination

RS: NVBS heard equally CVS: S1 S2 heard

CNS: NFND

PA: soft, non-tender, bowel sounds heard.

Local examination

Local examination showed left pre-auricular region.

Inspection

A solitary swelling of 3×4 cm approximately, oval in shape. Nodular surface, no visible scars or sinuses over the swelling, Skin over the swelling-normal.

Obliteration of retro mandibular groove+.

Palpation*:* No local rise of temperature. Non-tender. A solitary swelling of 3×4.5 cm, extending from posterior border of ramus of mandible to mastoid horizontally and vertically from lower border of ear lobule to 3 cm below. Surface- nodular. Firm in consistency. Plane of swelling-superficial to masseter muscle and freely mobile over the muscle. Bi digital palpation - deep lobe not palpable.

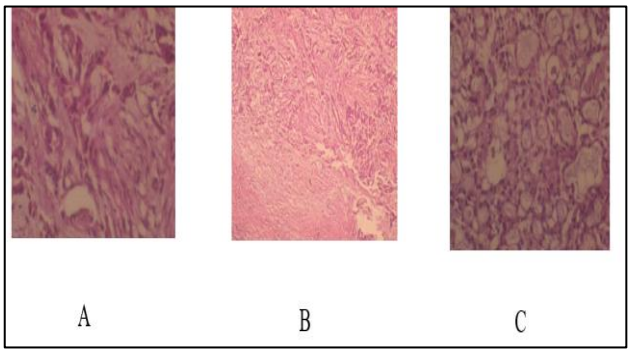

Figure 4: Microscopy.

Opposite parotid region: normal. Uvula: Central in position. No fullness or mass in tonsillar fossa or soft palate. Stenson duct opening: normal. Movement of jaw-normal and adequate mouth opening Nasolabial, angle of mouth (Both sides)-normal. No facial nerve weakness.

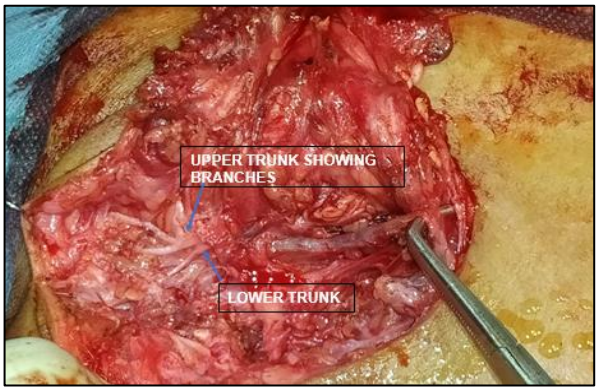

Figure 5: Intra operative picture demonstrating facial nerve branches.

Investigation

Routine investigations-within normal limits.

FNAC- F/S/O pleomorphic adenoma of parotid gland.

USG of parotid region shows well-defined combination of solid and cystic lesion measuring 2.4x1.5 cm with no lymph-node enlargement.

Diagnosis

Pleomorphic adenoma of left parotid gland.

Surgery

Superficial parotidectomy with identification and preservation of the facial nerve.

HPE report features suggestive of mammary analogue secretary carcinoma (pT1N0Mx) Advised IHC for confirmation: S100, mammoglobin, PK7, P53, calponin, EMA, vimentin to rule out cribriform cystadenocarcinoma and polymorphous adenocarcinoma that show similar histology. ETV6 rearrangement confirmation by FISH.

We lost follow up of the patient though we had planned for revision total parotidectomy.

DISCUSSION

MASC abbreviated as mammary analogue secretory carcinoma, is a fairly recent entity in salivary gland tumours defined by specific gene mutation namely ETV6 gene rearrangement. Having a similar histomorphology and immunohistochemical profile to secretary carcinoma breast, hence the name MASC. It is a rare tumour mainly occurring in young patients but not exclusive and carries a favourable prognostic outcome.[3]

A balanced chromosomal translocation t(12; 15) (P13; Q25) which leads to a fusion gene between the ETV6 gene on chromosome 12 and the NTRK3 gene on chromosome 15 is seen.[4] The biological consequence of the translocation is the fusion of the transcriptional regulator (ETV6) with membrane receptor kinase (NTRK3) that activates kinase through ligand-independent dimerisation and thus promotes cell proliferation and survival. The presence of ETV6-NTRK3 fusion gene has not been demonstrated in any other salivary gland tumour so far. The ETV6-NTRK3 translocation is not entirely specific for MASC, as it has been identified in a range of neoplasms including congenital fibrosarcoma, congenital cellular mesoblastic nephroma and acute myeloid leukaemia.[5]

Morphologically these tumour cells are composed of uniform cells arranged in micro cystic pattern, tubular pattern, solid sheets. The individual cells are bland looking with eosinophillic vacuolated cytoplasm and vesicular nuclei. The abundant secretions within the tubules are PAS positive.

Treatment and prognosis

The clinical course of conventional MASC is characterised by a moderate risk of localised recurrence (15%), lymph-node Metastasis (15%) and distant Metastasis (5%). Increase number of deaths preceded with local recurrence risk of which is more after simple enucleation than parotidectomy.[6] The stage at the time of diagnosis is the most important predictor of prognosis.

Unlike other tumours MIB1 proliferative index or any other search markers have not been studied. parotid gland mask MASC showing high-grade features was reported in three patients.[7] These cases had an accelerated clinical course associated with recurrence and metastasis resulting in death within 2 to 6 years of primary diagnosis.[7]

Based on few cases MASC is currently termed as a low-grade carcinoma with favourable prognosis. In comparison to its close differential acinic carcinoma MASE shows a slightly high risk of regional nodal metastasis.[6]

Treatment modality for high-grade transformed MASC involves radical surgery with adjuvant radiotherapy.

On diagnosing MASC Testing for ETV6 rearrangement is very essential for patient management particularly cases undergoing high-grade transformation, because this translocation may represent a therapeutic target. Recent studies show the inhibition of ETV6-NTRK3 activation serves as a therapeutic target for treatment. A recent study showed ETV6-NTRK3 fusion inhibitor as a prominent target of FDA approved drug crizotinib.[8] Offering a potential valuable treatment option for high grade and/or metastasising MASC.

CONCLUSION

Breast and salivary gland share similar architecture and cellular composition which enables them to have similar morphology and immuno profile. This in turn attributes to development of similar neoplastic lesions. MASC has characteristic recurrent balanced chromosomal translocation t(12;15) (p13;q25), resulting in ETV6-NTRK3 oncogenic fusion gene which encodes a chimeric tyrosine kinase. Clinical course is not much different than a benign disease, with moderate risk of localized recurrence (15%), lymph-node Metastasis (15%) and distant Metastasis (5%). Treatment modality is different for benign lesions and MASC. Superficial parotidectomy is suffice for a benign lesion, whereas treatment modality for high-grade transformed MASC involves radical surgery with adjuvant radiotherapy. Therefore, diagnosing MASC by testing for ETV6 rearrangement is very essential for patient management particularly cases undergoing high-grade transformation, because this translocation may represent a therapeutic target and aid in our treatment plan.

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